

REMARKS

This Amendment is respectfully submitted in response to the Office Action dated December 13, 2007. Claims 51, 54-56, 58-64, 66, 67, 69, 70 and 81-84 are pending in the application. Claims 51, 54-56, 58-63 and 81 are allowed. Claims 64 and 83 have been amended. The Commissioner is hereby authorized to charge deposit account 02-1818 for any fees which are due and owing.

Claims 64, 66, 67, 69, 70 and 82-84 were rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. Applicants have amended Claim 64 to establish antecedent basis for elements of Claim 64 and Claims 66 and 82 as recommended in the Office Action. Applicants have also amended Claim 64 to clarify that the method includes introducing into a neural precursor cell with a recombinant DNA construct comprising a receptor ligand-regulated *c-myc* cDNA to express a chimeric *c-myc* protein comprising a *c-myc* protein fused with at least one nuclear receptor protein having a *c-myc*-activating ligand binding domain. In addition, Claim 83 has been amended to clarify that the neural precursor cell is capable of differentiating into a neuron upon withdrawing the mitogen and the *c-myc* activating agent. Therefore, Applicants respectfully submit that the rejections under 35 U.S.C. §112, second paragraph, have been overcome and should be withdrawn.

Claims 64, 66, 67, 69, 70 and 82-84 were also rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter not described in the specification. The Office Action at page 3 suggests that there is inadequate support in the specification for claiming the use of anything but a MycER construct and β -estradiol as the *c-myc* activating agent to maintain the capacity of a neural precursor cell line of a human to differentiate into neurons *in vitro*. Applicants respectfully submit that it is clear from the specification that it is the genetic modification method with the *c-myc* gene that stabilizes neural precursors cell lines and that receptor-ligand systems other than the MycER/ β -estradiol system may be used to regulate *c-myc*.

Increasing the concentration of active *c-myc* protein leads to the generation of stable human CNS stem cell lines...(page 24 of the specification).

The ligand binding domain of these nuclear receptor proteins and their ligands can substitute for the estrogen receptor and β -estradiol

in order to regulate functions of the fused c-myc protein moiety.... Some receptor-ligand systems are better suited than others for the purpose of regulating the over-expressed c-myc... (page 26 of the specification)

The specification, for example, at page 26 provides a listing of various nuclear receptors and their respective ligands.

Examples of such nuclear receptors are glucocorticoid receptor, progesterone receptor, androgen receptors, vitamin D receptor, thyroid hormone receptors, retinoic acid receptors, and ecdysone receptor. Each of these receptors can be activated intracellularly by adding to the culture medium its appropriate ligands. Examples of the ligands are steroid hormones such as glucocorticoid or dexamethasone, thyroid hormones, retinoids such as retinoic acids, vitamin D, and the insect molting hormone, ecdysone, as well as their synthetic analogs designed to act on the respective receptors.

In fact, the specification provides at page 27 an example of a chimeric *c-myc* protein comprising a *c-myc* protein fused with a progesterone receptor protein having a *c-myc*-activating ligand binding domain.

One such potential system is human progesterone receptor and its antagonist ligand, RU38486....Thus, one enhanced *c-myc* expression system to produce stable cell lines would be to construct a plasmid in which the human *c-myc* gene is fused to the ligand binding domain of the human progesterone receptor...and to generate the intact retrovirus expressing the chimeric protein, *c-myc*-progesterone receptor (MycPR).

Therefore, the MycER construct and its receptor ligand, β -estradiol, is not the sole receptor-ligand system taught in the specification to maintain the capacity of a neural precursor cell line of a human to differentiate into neurons *in vitro*. Accordingly, Applicants respectfully submit that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn and that Claim 64 and the claims which depend therefrom are in condition for allowance.

An earnest endeavor has been made to place this application in condition for allowance and such allowance is courteously solicited. If the Examiner has any questions related to this Response, Applicants respectfully submit that the Examiner contact the undersigned.

Respectfully submitted,

BELL, BOYD & LLOYD LLP

BY

Bradley E. Davis
Reg. No. 56,727
Customer No. 24573
312-807-4409

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